Martini-Klinik experience on prostate cancer surgery during the early phase of COVID-19

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Introduction

In order to restrain an uncontrolled spread of the 2019 Coronavirus-Disease (COVID-19) and to provide sufficient intensive-care unit (ICU) capacity, medical specializations needed to develop new routines and risk-strategy protocols. Those restrictions have also impacted the urologic community. Several medical organisations developed specific information-hubs, blogs and resource centers on how to tackle the COVID-19 situation (1–3). Although the German Society of Urology ("DGU") has published a recommendation to evaluate the need for a timely therapy in prostate cancer (PCa) patients according to D'Amico risk groups on the 2nd of April 2020, up to now no compulsory directives exist regarding omitting radical prostatectomy (RP) during the COVID-19 pandemic. The Martini-Klinik Prostate Cancer Center (MK) at the University Hospital Hamburg-Eppendorf (UHH) continued surgery for PCa under risk-adjusted special precautions. In this study, we share our initial experiences, routines and results of patients in the early COVID-19 phase.

Patients and methods

After approval of the study by the institutional review board, we performed a retrospective analysis of patient and preoperative tumor characteristics, as well as short-term complications of PCa patients undergoing RP at our institution before and during the early phase of the COVID-19 pandemic in Germany. One group represented a consecutive cohort of treated PCa patients since the first COVID-19 case at UHH was detected (27th February 2020 – 17th April 2020), while the second

group represented consecutive patients treated before the first event (1st January – 26th February 2020).

We evaluated possible short-term postoperative complications and circumstances which occurred in relation to COVID-19. Presumably predisposing factors for a potentially worse outcome in case of infection or increasing the probability to be depended on postoperative ICU care (focusing on patient age, cardiovascular disease and hypertension, obstructive sleep apnoea syndrome (OSAS), diabetes mellitus, chronic lung, kidney or liver disease and severe obesity) have been assessed by evaluation of patient history. All analyzed patients gave their informed consent for data-analysis. All clinical and patient data was stored in a secured and pseudonymized database in the MK.

COVID-19 measures of the University Hospital Hamburg/Martini-Klinik

Within close communication to the official German public health institute "RKI" (Robert-Koch Institute) (4), a task force has defined the procedures and safety measures for all sections of the UHH, thus including the MK, since the first COVID-19 patient in Germany. Besides being physically "disconnected" from the main complex of the UHH and offering only one- and two-bed rooms, thus profiting from certain advantages in terms of infection control, further measures were established in the MK in concordance with the task force. Routinely, no COVID-19 testing was performed prior to surgery. However, before hospital admission and again prior to surgery, patients were repetitively asked about COVID-19 exposure or symptoms **(see supplementary material).** Patients with potential COVID-19 exposure were only admitted after a symptom free period of > 14 days and negative testing. Further COVID-19 measures of the UHH task force and the MK can be depicted in **figure 1.**

Considerations on statistical analyses

Descriptive statistics of categorical variables focused on frequencies and proportions. Medians and interquartile ranges (IQR) were reported for continuously coded variables. For all statistical analyses R software environment for statistical computing (version 3.4.3) was used. All tests were two sided with a level of significance set at $p < 0.05$.

Results

We compared results of 447 patients treated prior to the COVID-19 pandemic versus 337 patients during the early COVID-19 phase. Patient characteristics including preoperative tumor characteristics were comparable. Further results are depicted in **table 1.**

26 planned surgeries have been postponed or cancelled due to the COVID-19 situation. First COVID-19 related prophylactic cancellations of surgeries in the MK occurred on March 12th. Two planned patients were confirmed COVID-19 positive (by their general practitioners) before admission to the MK. Surgery of 13 patients was postponed due to a high risk for inheriting a COVID-19 infection. 11 patients cancelled due to the fear of the COVID-19 situation in general. No patient with confirmed COVID-19 has been present within the MK up to now. Of 230 staff members of the clinic, 31 have been tested for COVID-19, mainly due to returning from RKI declared COVID-19 risk regions after vacation or business travel. One MK ward nurse was confirmed COVID-19 positive on April 21st without evidence of the origin of infection. After having created contact lists, all staff members and patients who have been in contact with the nurse have been tested and their results were negative.

Intensive care occupancy during early COVID-19 phase

We have noted a slight decrease in the number of ICU transfers during the early COVID-19 phase (n = 19; median 2/week, IQR 0-2.25) compared to the pre-COVID phase (n = 26; median 3/week, IQR 2.75-3.25).

The main reason for ICU transfers was a precautionary relocation, prompted by institutional standards of the anesthesiology department, in order to ensure monitoring for patients who were not assumed fit enough for the ward. Those relocations lasted only for the first postoperative night and retransfer to MK was arranged on the first postoperative day. Two patients during the COVID-phase however were relocated to the ICU due to Clavien IV complications (pulmonary embolism and hemorrhagic shock)

Short-term complications due to COVID-19

Since no COVID-19 case occurred in our clinic during the early phase, we were unable to identify COVID-19 related complications in our patients. Moreover, we

could not identify a connection to potentially concealed COVID-19 infections. Further short-term surgical complications are depicted in **table 1.**

Discussion

Our data is an excerpt to demonstrate the feasibility to continue surgery for PCa in a prepared surrounding. However, we acknowledge that the precautions and measures we have implemented within the MK might differ to other institutions or countries. This was mainly possible due to fact that the German health system and specifically the UHH provide an extraordinary hospital bed and ICU capacity, which gave a certain leeway especially in this early phase of COVID-19. Furthermore, the MK is in the special situation to be physically not connected to the main UHH complex of buildings and therefore, we were able to treat our patients in a reasonably protected surrounding. As we usually do not discharge patients before having them monitored for at least three days after surgery, we were able to recognize potential early COVID-19 related complications. If any signs of overstressing the UHH capacity had occurred, we would have taken the consequence to drastically decrease our activity. If necessary, the MK would have (and will) provide its bed-capacity to intercept a potential uncontrollable situation.

Of note, we did not perform COVID-19 screening routinely but rather trusted in thorough and repeated assessment of patient history prior to admission to the clinic. Speaking of the general population, the RKI initially recommended testing only for patients with explicit symptoms and those with a very high risk of harboring COVID-19 (e.g. people in close contact to a confirmed case), while in later days, due to the increased availability of tests, recommendations are to test also mildly symptomatic persons. Very recently we decided to perform in-house reverse real time reverse transcription–polymerase chain reaction tests (RT PCR) for all patients admitted to MK prior to surgery.

We are aware that this virus is unpredictable and therefore, most likely further adjustments of our actions have to be considered in the future in order to decrease the probability of a further spread and potentially avoidable complications or deaths. Although it is undisputed that cancer surgery cannot be postponed indefinitely, a certain delay in treatment of PCa due to the COVID-19 pandemic might not influence oncological outomes (3,5). Nevertheless, mainly due to the rapid roll of events during the early advent of the virus in Germany, we continued to perform surgeries for all

risk-groups as most of these patients have already been diagnosed before and already enrolled on a waiting-list for a longer period. Therefore, we decided to continue to treat also patients with low-risk cancer in very fit patients and a life expectancy far beyond 10 years. However, in this scenario, reserving surgery for patients with more aggressive tumor features most likely finds the biggest agreement in the future, as this has also been advocated recently by the European Association of Urology (EAU) (3). Further surgical measures will be taken into consideration, such as the latest EAU Robotic Urology Section guideline advocating the reduction of potentially contagious airborne viral particles within the operating room (6).

Conclusion

In the early phase of COVID-19, we experienced a favorable outcome of our patients, without having taken rigorous screening measures apart from a thorough patient history and by applying strict protective hygiene standards.

Acknowledgements

We would like to thank all involved institutions which enable the MK to provide the necessary care to our cancer patients during the COVID-19 pandemic. Furthermore, we would like to distance ourselves of a general recommendation to commence surgery in other institutions or countries despite our favorable data. Nevertheless, we hope that our data contributes to a constructive discussion on possible future strategies within the medical community.

Conflicts of interest

none

Figure legends

Figure 1:

Measures taken by University Hospital Hamburg-Eppendorf (UHH) and the Martini-Klinik Prostate Cancer Center (MK) since the first positive COVID-19 case in Germany on 27th of January 2020. For further comprehension, weekly numbers of

COVID-19 infections in Germany and the city of Hamburg as well as hospitalized patients at the UHH have been added, based on official numbers of the Robert Koch Institute and the UHH task force.

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Variables		Overall	Pre COVID-19	COVID-19	p-value
Age [years]	Median (IQR)	64 (58.8-69)	64 (58-68)	64 (59-69)	0.89
BMI [kg/m^2]	Median (IQR)	26.5 (24.7-29.1)	26.6 (24.8-29.1)	26.3 (24.5-28.7)	0.30
PSA [ng/ml]	Median (IQR)	7.6 (5.5-11.8)	7.5 (5.4-12)	7.6 (5.5-11.6)	0.82
ISUP Grading [biopsy], n (%)	I	187 (23.9)	105 (23.5)	82 (24.3)	0.16
	II	291 (37.1)	165 (36.9)	126 (37.4)	
	III	145 (18.5)	82 (18.3)	63 (18.7)	
	IV	89 (11.4)	53 (11.9)	36 (10.7)	
	V	59 (7.5)	30 (6.7)	29 (8.6)	
	NA	13 (1.7)	12 (2.7)	1 (0.3)	
Comorbidities*, n (%)	yes	418 (53.3)	248 (55.5)	170 (50.4)	0.18
	no	366 (46.7)	199 (44.5)	167 (49.6)	
ASA score, n (%)	I	56 (7.1)	36 (8.1)	20 (5.9)	0.40
	II	613 (78.2)	341 (76.3)	272 (80.7)	
	III	111 (14.2)	67 (15)	44 (13.1)	
	IV	1 (0.1)	1 (0.2)	0 (0)	
Surgical approach, n (%)	RARP	455 (58)	257 (57.5)	198 (58.8)	0.77
	ORP	329 (42)	190 (42.5)	139 (41.2)	
LOS [days]	Median (IQR)	7 (6-8)	7 (7-8)	7 (6-8	<0.01
Complications**, n (%)	I	56 (7.1)	35 (7.8)	21 (6.2)	0.63
	II	70 (8.9)	44 (9.8)	26 (7.7)	
	IIIa	22 (2.8)	14 (3.1)	8 (2.4)	

	IIIb	13 (1.7)	8 (1.8)	5 (1.5)	
	IVa	7 (0.9)	5 (1.1)	2 (0.6)	
	none	616 (78.6)	341 (76.3)	275 (81.6)	

Table 1

Patient and tumor characteristics of 447 patients treated prior to the COVID-19 pandemic versus 337 patients during the early COVID-19 phase at the Martini-Klinik Prostate Cancer Center Hamburg.

**Comorbidities: predisposing factors for a potentially worse outcome in case of a COVID-19 infection or increasing the probability to be depended on postoperative ICU care, such as cardiovascular disease, hypertension, obstructive sleep apnoea syndrome (OSAS), diabetes mellitus and chronic lung, kidney or liver disease.*

*** Complications according to the Clavien-Dindo Classification*

Abbreviations:

BMI	*Body mass index*	*LOS*	*Length of stay*
RARP	*Robot-assisted radical prostatectomy*	*PSM*	*Positive surgical margin*
ORP	*Open retropubic radical prostatectomy*	*PSA*	*Prostate specific antigen*
ISUP	*International Society of Urological Pathology*		
ASA	*American Society of Anaesthesiologists Scoring*		

Figure 1

Time period	Infections Germany	Infections Hamburg (*)	Infections UHH**
on 27 Feb	<100	1	1
02 Mar - 08 Mar	262	3	1
09 Mar - 15 Mar	4838	162 (8.8)	2
16 Mar - 22 Mar	18.610	872 (47)	18
23 Mar - 29 Mar	52.547	1846(100)	36
30 Mar - 05 Apr	91.714	2945 (160)	35
06 Apr - 12 Apr	120.479	3742 (203)	53
13 Apr - 19 Apr	139.897	4167 (226)	48

(*) COVID-19 cases per 100.000
*** inpatient treatment at the UHH*

General measures at UHH:

- Quarantine and strict testing for staff members of high risk for infection
- No further business travelling allowed
- Visiting ban at UHH
- Increase ICU capacity from 120 to 150 beds
- Establish an explicit department for assessing upper respiratory tract symptoms
- Reduce surgical and conservative procedures by 50% (focus on urgent/oncological procedures)
- Hold 60% free beds throughout the UHH
- Mandatory wearing of protective face masks for all staff members in contact with any patient (Non FFP2-3; except for contact with COVID-19 patients)

Specific measures at MK:

- Reduction of surgical program (12→10 RP's)
- RP's only on the MK premises (to reduce fluctuation to UHH OR's)
- Mandatory wearing of face masks (non FFP2-3) in the OR and wards, also in non-septic areas
- Permanently fixed anaesthetics team in the MK
- "Online-morning briefing" for medical staff
- Telephone consultation replaced regular outpatient consultations
- Centralization of all patient admissions to one specific sector within MK
- No elective postoperative x-ray cystography to exclude anastomosis leakage (which was also usually performed within the main UHH complex)
- If possible, try to reduce length of stay
- Critically assess comorbidities which potentially absorb ICU capacity in the acute postoperative phase (*cardiovascular disease; hypertension; diabetes mellitus; asthma; chronic lung, kidney or liver disease; severe obesity; OSAS)*

OSAS precautions included:

- *OSAS with own CPAP mask: surgery possible if no other relevant restrictive comorbidities are present*
- *OSAS without own CPAP mask: surgery was postponed*
- *STOP-Bang Score[1] > 4: surgery possible under special circumstances: extended anesthesiologic supervision of the patient in the recovery room until at least 9 p.m.; then, continuous monitor surveillance was performed by a specifically trained nurse*

Abbreviations:

COVID-19	*Corona Virus Disease 2019*	*RP*	*Radical Prostatectomy*
UHH	*University Hospital Hamburg-Eppendorf*	*ICU*	*Intensive care unit*
OR	*Operating room*	*CPAP*	*Continuous positive airway pressure*
FFP	*Filtering face piece*	*OSAS*	*Obstructive Sleep Apnoea Syndrome*
MK	*Martini-Klinik Prostate Cancer Center*		

[1] *"snoring, tiredness, observed apnea, high blood-pressure, BMI, age, neck circumference, and male gender (STOP-Bang) questionnaire" to screen for potential OSAS was applied for all patients admitted to the MK.*